REMARKS

Applicants thank the Examiner for directing their attention to allowable subject matter in the Office Action dated May 6, 2005. In keeping with the spirit of the allowable subject matter indicated, Applicants have submitted new claims 102-113. Applicants also thank the Examiner for the helpful discussion in the teleconference of August 9, 2005 regarding methods directed to the use of compositions consisting essentially of a batimastat compound and polymeric suspension agents, and accordingly submit new claims 90-101.

Provisional Non-Statutory Double Patenting

Applicants thank the Examiner for previously holding the Non-Statutory Double Patenting rejection in abeyance. Applicants respectfully submit that as this application is now in condition for allowance, the double patenting rejection should be withdrawn and the application permitted to pass to allowance in keeping with MPEP 804(I)(B). Withdrawal of the rejection is in keeping with MPEP 804(I)(B) because co-pending application 09/648,446 has not issued and a non-provisional Non-Statutory Double Patenting rejection cannot be maintained.

In the event this Application does not pass to allowance, Applicant's respectfully request the Examiner to continue to hold the provisional Non-Statutory Double patenting rejection in abeyance until allowable subject matter is identified. Applicants will address the merits of the double patenting rejection in the appropriate application.

Rejection under 35 U.S.C. § 112 ¶ 2

Claims 67 and 69 have been cancelled, thereby rendering the Examiner's concerns moot. In view of the foregoing, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112 ¶ 2.

Rejection under 35 U.S.C. § 102

Claims 7-12, 14, 23-30, 32, 38-42, 69, and 70 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent 5,767,153.

Applicants respectfully submit that the cancellation of claims 7-70 renders the rejection moot with regard to the previously pending claims. To the extent that the Examiner may allege that the newly presented claims set forth a "one step method of preventing retinal neovascularization" that is anticipated by the '153 reference, Applicants addressed the matter below.

Anticipation requires that a single prior art reference disclose each and every limitation of the claimed invention. *Lewmar Marine, Inc. v. Barient, Inc.*, 827 F.2d 744, 747 (Fed. Cir. 1987). However, a prior art reference may anticipate a claim without expressly disclosing a feature of the claimed invention if that missing feature is necessarily present, or inherent, in the single anticipating reference. *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991). In order for the Examiner to rely on inherency of disclosure to support a rejection, "the Examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990);

M.P.E.P. § 2112 (emphasis in original); see also *In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1351 (Fed. Cir. 2002).

Applicants respectfully submit that the '153 reference does not present a novelty bar to claims directed to "...method for treating (or preventing) retinal neovascularization in a mammal... ." The Examiner alleges that the '153 reference "... teaches the topical administration to a recipient of a composition comprising batimasatat (0.3 weight %) and polycarbophil (1.15% weight %)."[1] Stating that the reference does *not* provide a disclosure of "... treatment of retinal neovascularization" by topical administration of the recited composition,[2] the Examiner relies upon inherency of disclosure to raise the inference that the missing limitations necessarily flow from the '153 disclosure in order to find anticipation under § 102(b).

Whatever else the Examiner has shown, the Examiner has failed to show that the instant methods of preventing retinal neovascularization, necessarily flow from the '153 patent disclosure. The Examiner's allegation that claims directed to prevention (prophylaxis) are inherently taught by the '153 reference as the inherent result of a one step method fail for more than one reason. First, the allegation fails because as stated by the Examiner the reference fails to teach "treatment of retinal neovascularization" prophylactic or otherwise. Second, just because a mammal is susceptible to a condition does not mean that they are in need of prophylaxis. Third, the Examiner has not established that a person practicing the method of the '153 patent would necessarily be treating a subject prophylactically, and thus treatment for the

[1] Office Action of October 8, 2004 at page 3.

[2] Office Action of October 8, 2004 at page 5; Office Action of May 6, 2005, at page 6.

purpose of preventing retinal neovascularization would not necessarily be encompassed explicitly or inherently by the '153 reference.

The Examiner further relies upon the decision in *Titanium Metals v. Banner*, 778 F.2d 775 (Fed. Cir. 1985) to support the assertion that the '153 patent may be employed as an anticipatory reference. The Examiner's reliance upon the decision in *Titanium Metals* is mistaken. As recognized by the Examiner,[3] the decision in the *Titanium Metals* case was directed to the patentability of product claims (titanium alloys) over a disclosed product,[4] and ***not*** the patentabilty of novel methods of using a product over a disclosed product. Whatever else the decision in *Titanium Metals* may stand for, it **does not** stand for the proposition that a prior recitation of a product supports the rejection of undisclosed methods of using that product based upon inherency.

Rejection under 35 U.S.C. § 103

Claims 1-42, and 67-70 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over US 5,767,153 in view of WO 97/41844.

The Examiner bears the initial burden of establishing a *prima facie* case of obviousness under 35 U.S.C. § 103, *In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988), in which the prior art references applied must teach or suggest all of the claim limitations. *In re Royka,* 409 F.2d 981, 984 (CCPA 1974). In addition, there must be some suggestion or motivation to modify or combine references and there must be a reasonable expectation of success, *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). Both the suggestion or motivation to make the claimed combination,

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[3] Office Action of October 8, 2004, at page 4.

[4] *Titanium Metals v. Banner*, 778 F.2d 775, 781 (Fed. Cir. 1985).

and the reasonable expectation of success, must be found in the prior art, and not based on the Applicant's disclosure. *In re Vaeck*, 947 F.2d at 493.

The Examiner has taken the position that the previously pending claims are obvious in view of the combination of the '153 reference and the '844 reference. Applicants respectfully maintain that the '844 reference, alone or in combination with the '153 reference, did not render obvious the previously presented claim as the references do not teach all of the limitations of the claims, and there exists neither a motivation to combine the references nor a reasonable expectation of success to derive Applicant's invention. In particular, Applicants maintain that the '844 reference does not teach topical ophthalmic administration to the eye to achieve treatment of the retina. [5] In order to advance prosecution, however, Applicants have amended their claims to obviate any rejection of previously pending claims 1-6, and new claims 71 - 113.

a. The '844 reference alone or in combination with the '153 reference does not teach all of the limitations of the claims

Applicants respectfully submit that the '844 reference, alone or in combination with the '153 reference cannot render obvious amended claims 1-6 and newly presented claims 71- 113. Whatever else the '844 reference teaches, it neither teaches nor fairly suggest methods for treating (or preventing) retinal neovascularization in a mammal in need of such treatment,

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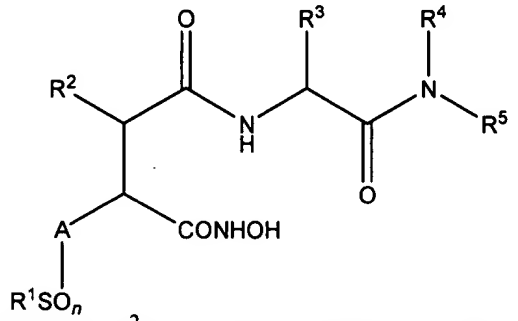
[5] The Examiner has previously rejected the argument that the Geroski reference supports the assertion that a skilled artisan would have no reasonable expectation of success in arriving at Applicants' invention. Specifically, the Examiner asserts that the Geroski reference is not persuasive because it states "topical formulations remain effective because of the very high concentration of drugs that are administered." See the Office Action dated 10/8/2004 at page 7. Applicants respectfully submit that the passage relied upon by the Examiner refers only to administration to the ***anterior*** **tissues** of the eye; **the *retina* is a tissue of the *posterior segment* of the eye**. Moreover, the Geroski reference makes it clear that "the treatment of posterior segment diseases is to a significant extent limited by the difficulty in delivering effective doses of drugs to target tissues in the posterior eye." See, page 961, column 2, lines 1-3 of the Geroski reference.

comprising topically administering to the eye a composition capable of delivering a therapeutically effective amount of a batimastat compound to the retina, as recited in amended claim 1, and new claim 78 that recite comprising a polymeric suspension agent which suspends a therapeutic agent, said therapeutic agent consisting essentially of a batimastat compound of the formula:



where R^1 represents thienyl, R^2 represents a hydrogen atom or a C_1-C_6 alkyl, C_1-C_6 alkenyl, phenyl(C_1-C_6) alkyl, cycloalkyl(C_1-C_6)alkyl or cycloalkenyl(C_1-C_6)alkyl group, R^3 represents an amino acid side chain or a C_1-C_6 alkyl, benzyl, (C_1-C_6 alkoxyl)benzyl or benzyloxy(C_1-C_6 alkyl) or benzyloxy benzyl group, R^4 represents a hydrogen atom or a C_1-C_6 alkyl group, R^5 represents a hydrogen atom or a methyl group, n is an integer having the value 0, 1 or 2, and A represents a C_1-C_6 hydrocarbon chain, optionally substituted with one or more C_1-C_6 alkyl, phenyl or substituted phenyl groups, or a salt thereof; and a derivative of batimastat formed by methylation halogenation, acetylation, esterification and hydroxylation.

Moreover, whatever else the '844 reference teaches, it neither teaches nor fairly suggest methods for treating (or preventing) retinal neovascularization in a mammal in need of such treatment, comprising topically administering to the eye a composition capable of delivering a therapeutically effective amount of a batimastat compound to the retina wherein said composition either "**consisting essentially of** a polymeric suspension agent and a batimastat compound of the formula...," or "**consisting of** a polymeric suspension agent and a batimastat compound of the formula ...," as recited in independent claims 90 and 102.

Further to the foregoing, Applicants respectfully submit that the '153 reference cannot makeup for the deficiencies of the '844 reference, because as the Examiner has stated, "[t]he reference lacks disclosure of use of the composition of polycarbophil and batimastat for the treatment of retinal neovascularization."

b. There is no motivation to combine the '153 and '844 references.

The Examiner contends that the cited art teaches the motivation to substitute the compositions of the '153 patent into methods of treating retinopathies allegedly taught in WO 97/41844 (the '844 reference).[6] Applicants respectfully disagree. The claims are directed to methods "for treating (or preventing) retinal neovascularization in a mammal in need of such treatment, comprising topically administering to the eye a composition capable of delivering a therapeutically effective amount of a batimastat compound to the retina, said compositions either "comprising a polymeric suspension agent which suspends a therapeutic agent, said therapeutic agent consisting essentially of a batimastat compound of the formula..." as recited in independent claim 1 and 78, or consisting essentially of a polymeric suspension agent and a batimastat compound . . . " as recited in claim 90.[7] Whatever else the '844 reference teaches it neither teaches nor fairly suggests the use of such compositions, as it is directed to compositions comprised of two or more angiostatic agents. In this regard, the '844 reference states "[s]pecifically, the invention is directed to compositions containing two or more angiostatic agents. . . ."[8] In view of the foregoing, the '844 reference provides no motivation to combine the references and derive a method employing a single angiostatic agent as in the instant claims.

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[6] Office Action dated March 8, 2004 at page 3.

[7] Applicants note the Examiner suggested the "consisting of" language employed in independent claim 102 was allowable over the art of record on the Office Action dated May 6, 2005.

[8] *See e.g,* WO 97/41844 page 1, lines 13 – 15, and page 4, lines 21-22.

c. The '844 reference teaches away from its combination with the '153 reference.

To establish a *prima facie* case of obviousness, "some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references." must be shown. *See, e.g., In re Fine,* 837 F.2d 1071, 1074 (Fed. Cir. 1988). No suggestion to combine references exists if a reference teaches away from its combination with another source. *See id* at 1075. "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, . . . would be led in a direction divergent from the path that was taken by the applicant . . . ." *Tec Air Inc. v. Denso Mfg. Mich. Inc.*, 192 F.3d 1353, 1360 (Fed. Cir. 1999) (quoting In re Gurley, 27 F.3d 551, 553 (Fed.Cir.1994)).

Applicants respectfully submit that the '844 reference teaches away from the instant invention because a person of ordinary skill would be led in a direction divergent from the path that was taken by the Applicants. In this regard, the claims are directed to methods for treating (or preventing) "retinal neovascularization in a mammal in need of such treatment, comprising topically administering to the eye a composition capable of delivering a therapeutically effective amount of a batimastat compound to the retina." The compositions set forth in the amended claims either "comprising a polymeric suspension agent which suspends a therapeutic agent, said therapeutic agent consisting essentially of a batimastat compound of the formula...," "consisting essentially of a polymeric suspension agent and a batimastat compound..." or "consisting of a polymeric suspension agent, a batimastat compound...." As discussed above, the '844 reference teaches the use of "two or more" angiostatic agents in combination to treat neovasclarization,[9] because "current therapy for treatment of ocular neovascular disease is not very effective."[10] Since the '844 reference teaches using a combination of angiostatic agents, a skilled artisan

[9] Id.

[10] Id at page 2, lines 13-14.

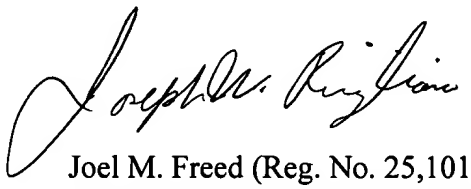
would not be led in the direction of using the compositions recited in the claims that have a single antiangiogenic batimastat compound. Thus, the '844 reference teaches away from the instant invention. As a reference that teaches away from the claimed invention cannot support a finding of obviousness in combination with another reference,[11] Applicants respectfully submit that the claims as presently amended obviate any rejection under 35 U.S.C. § 103 over the '844 reference.

For the above reasons, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 103(a).

CONCLUSION

In view of the foregoing Applicants believe the application is in condition for allowance and solicit a Notice of Allowance indicating such at the earliest possible time. The Examiner is encouraged to contact the undersigned should any additional information be necessary.

Respectfully submitted,



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**Not admitted to the practice of law. Admitted to practice before the U.S. Patent & Trademark Office only.*

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[11] *See, e.g., In re Fine,* 837 F.2d 1071, 1075 (Fed. Cir. 1988).